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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,810	07/13/2001	Paul Rennert	A068 US	6397

7590 02/11/2004

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EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/905,810	RENNERT, PAUL	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-9,12-15 and 23* is/are pending in the application.

4a) Of the above claim(s) *6-9 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,12-14 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 11/21/2003, is acknowledged.

2. Claims 1, 4-9, 12-15 and 23 are pending.

3. Claims 6-9 and 15 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 1,4-5 and 12-14 and 23 are under examination as they read on a method for blocking the development or treating or reducing the severity or effects of an immunological disorder comprising administering an antibody directed against the TWEAK ligand wherein the immunological disorder is GVDH and organ transplant failure resulting from graft rejection.

5. In view of the amendment filed on 11/21/2003, only the following rejection is remained.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 4-5, 12-14 and 23 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for blocking the development or treating or reducing the severity or effects in a subject having graft-versus-host disease or an organ transplant failure resulting from allograft rejection in a human comprising administering antibody against human TWEAK ligand of SEQ ID NO: 2, wherein said Graft-versus-Host Disease is caused by a combination of a Th1 and a Th2 cell-mediated immune response does not reasonably provide enablement for a method for blocking the development or treating or reducing the severity or effects of a GVHD in anY animal comprising the step of administering any pharmaceutical composition which comprises a therapeutically effective amount of an anti-TWEAK polypeptide monoclonal antibody and a pharmaceutically acceptable carrier, wherein said Graft-versus-Host Disease is caused by a combination of a Th1 or a Th2 cell-mediated immune response alone in claims 1 and 12-13; or a method for blocking the development or treating or reducing the severity or effects of **any organ transplant failure resulting from graft rejection** in an animal comprising the step of administering any pharmaceutical composition which comprises a therapeutically effective amount of an anti-TWEAK polypeptide monoclonal antibody and a pharmaceutically acceptable carrier in claim 1, wherein the immune response is a Th1 cell-mediated immune response in claim 12, a Th2 cell-mediated immune response in claim 13 or both a Th1 and a Th2 cell-mediated immune response in claim 14. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make and/or use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action, mailed 05/21/2003.

Applicant's arguments, filed 11/21/2003, have been fully considered, but have not been found convincing

The specification provides no direct or indirect relationship between Th1 or Th2 and anti-TWEAK antibody in the method for blocking the development or treating or reducing the severity or effects of a GVSD or organ transplant failure resulting from graft rejection. Applicant's arguments are directed to the effects of Th1 and Th2 on GVSD but missing the relationship between those cells and anti-TWEAK antibody relationship. Further, the specification on page 8, lines 1-7, discloses that the TWEAK biology is as yet only partly understood. The specification further discloses that soluble TWEAK induces the chemokine IL-8 secretion in HT29 colon and A375 malignant melanoma cell lines, but fails to provide guidance on the effect of anti-TWEAK antibody on the Th1 and/or Th2 cells and IL production. Furthermore, Applicant concluded on page 16, lines 5-9, of the amendment filed 11/21/2003, that the cited references demonstrate that one factor influencing the development of either acute or chronic GVHD involves the development of an immune response to foreign non-self antigens and "a critical balance between the cytokines generated by CD4+ Th1 and Th2 cells". Applicant appears to admit that both Th1 and Th2 are required in GVHD response. Given Dallman (Current opinion in Immunology 7:632-638, 1995, off record) teachings that both Th1 and Th2 cells are involve in graft rejection response. In addition to Dallman's conclusion that it is difficult to make a case that graft rejection is caused by an immune response driven by either Th1 or Th2 cells alone (see page 632). One skilled in the art at the time the invention was made would not know whether the GVHD resulted from Th1, Th2 or both mediated immune response. The specification lacks direction or objective evidence as to which T helper type is responsible for the immune response in GVHD using anti-TWEAK antibody.

Further, the specification is not enabled for organ unrelated (xenografts) transplant failure, which leads to more damage or/and destruction of the grafted organs, wherein the level of immune suppression and/or rejection is expected to be greater in xenograft recipients. The specification fail to provide sufficient guidance enable the treatment and development of a xenograft rejection.

Furthermore, the amendment filed 11/21/03 amend the claim 1 to recite "antibody that binds specifically to a TWEAK ligand of SEQ ID NO: 2", it is noted that SEQ ID NO: 2 represents a human TWEAK ligand. A person of skill in the art would not be able to determine without undue experimentation whether the antibody that binds specifically to human ligand would share the ability to inhibit block the development or treat or reduce the severity or effects of GVHD or an organ transplant failure resulting from graft rejection in any animal, other than human.

8. No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (571) 272-0845. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (571) 272-0841. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9307.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
February 5, 2004

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600